

# Use of a postoperative insulin protocol decreases wound infection in diabetics undergoing lower extremity bypass

Fuyuki Hirashima, MD,<sup>a</sup> Reshma B. Patel, MD,<sup>a</sup> Julie E. Adams, MD,<sup>b</sup> Daniel J. Bertges, MD,<sup>b</sup> Peter W. Callas, PhD,<sup>c</sup> Georg Steinthorsson, MD,<sup>b</sup> Janet McSorley, APRN,<sup>b</sup> and Andrew C. Stanley, MD,<sup>b</sup> *Burlington, Vt*

**Objective:** Strict glucose control in patients undergoing coronary bypass grafting has been shown to decrease infectious complications, arrhythmias, and mortality. Our objective was to determine if strict glucose control reduced morbidity after lower extremity bypass (LEB).

**Methods:** A prospective pilot study at a single institution within the Vascular Study Group of New England was conducted from January 2009 to December 2010. Patients with diabetes and without undergoing LEB were placed on an intravenous (IV) insulin infusion for 3 days after surgery with titration of blood glucose from 80 to 150 mg/dL. The IV insulin study group (n = 104) was compared to a historic control group (n = 189) that received standard insulin treatment from the preceding 3 years. The Fisher exact test, *t*-tests, Wilcoxon rank-sum tests,  $\chi^2$ , and logistic regression analyses were used to compare in-hospital morbidity. Stratified analyses were conducted to determine if findings differed based on the presence or absence of diabetes.

**Results:** There was no difference in postoperative complications between the two groups with regard to graft infection, myocardial infarction, dysrhythmia, primary patency at discharge, or mortality. Patients in the IV insulin group had significantly fewer in-hospital wound infections (4% vs 11%; odds ratio [OR], 0.32; 95% confidence interval [CI], 0.11-0.96; *P* = .047). This association strengthened after adjusting for potentially confounding baseline differences in gender, body mass index, and smoking status (adjusted OR, 0.22; 95% CI, 0.05-0.84; *P* = .03). When stratified by presence of diabetes, wound infections were decreased in the IV insulin group (0/44 [0%] vs 9/90 [10%]; *P* = .03). In patients without diabetes treated with IV insulin, there was no significant difference in wound infections (7% vs 12%; *P* = .42).

**Conclusions:** Strict glucose control with a postoperative insulin infusion protocol significantly decreased the incidence of postoperative in-hospital wound infection in the diabetic population. These previously unreported findings from this single-institution prospective study warrant further investigation. (*J Vasc Surg* 2012;56:396-402.)

Recent literature has demonstrated the effectiveness of glucose control protocols in reducing complications in both coronary artery bypass grafting (CABG) and complex patients in the intensive care unit. Protocols vary, but, in general, use frequent blood glucose monitoring and the use of intravenous (IV) insulin to better control serum glucose. In particular, reductions in mortality after CABG, intensive care unit mortality, and infectious complications were observed when these measures were instituted.<sup>1-3</sup> Other studies have documented reductions in postoperative cardiac

complications with these protocols in place.<sup>4</sup> Some studies have reported complications related to the use of these protocols such as strokes, hypoglycemic events, and heart block requiring a pacemaker, leaving the potential risks and benefits of strict glucose control still under debate.<sup>5,6</sup> Theoretically, better glucose management should reduce complications. A number of hypotheses have been postulated regarding the mechanisms by which diabetes exerts its negative effects on vascular physiology. Diabetes has been correlated with altered macrophage and neutrophil function,<sup>7,8</sup> endothelial dysfunction,<sup>9</sup> decrease in nitric oxide synthesis,<sup>10</sup> and increase in the production of the vasoconstrictor endothelin-1.<sup>11</sup> Wound healing is compromised due to the microvascular effects of diabetes and alterations in inflammatory response.<sup>12</sup> It follows that by using a more aggressive approach toward glucose normalization in the postoperative patient, some of the pathologic side effects of the diabetic state, particularly wound and cardiac complications, should be avoidable. National attention on hospital-acquired infections has been the basis for studies that document various risk factors for infection.<sup>13</sup> Appropriate skin preparations, administration of antibiotics, type of surgery, indications for surgery (treatment of infection), and surgical technique all play a role in expected rates of

From the Department of Surgery,<sup>a</sup> Division of Vascular Surgery,<sup>b</sup> and Department of Medical Biostatistics,<sup>c</sup> University of Vermont.

This study was partially funded by James M. Jeffords Institute for Quality and Operational Effectiveness.

Author conflict of interest: none.

Presented at the Thirty-eighth Annual Meeting of the New England Society for Vascular Surgery, Providence, RI, September 16-18, 2011.

Additional material for this article may be found online at [www.jvascsurg.org](http://www.jvascsurg.org).

Reprint requests: Fuyuki Hirashima, MD, Department of Surgery, Fletcher Allen Health Care, 111 Colchester Avenue, Burlington, VT 05404 (e-mail: [fuyuki.hirashima@vtmednet.org](mailto:fuyuki.hirashima@vtmednet.org)).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214/\$36.00

Published by Elsevier Inc. on behalf of the Society for Vascular Surgery.

doi:10.1016/j.jvs.2012.01.026

infection complications.<sup>14,15</sup> The risk and avoidance of infection is clearly multifactorial and complex.

Patients undergoing lower extremity bypass (LEB) surgery are particularly at risk for postoperative cardiac complications as well as wound and graft complications. Recent center interval reports from the Vascular Study Group of New England (VSGNE) database found wound complication rates at our center and other centers in New England to be in the 10% to 12% range and the risk of cardiac complications (arrhythmias, myocardial infarctions, and congestive heart failure) to be in the range of 10% as well.<sup>16,17</sup> We conducted a single-center, nonrandomized, prospective, pilot study within the VSGNE to examine the effect of an IV insulin protocol on all patients undergoing LEB. It was our hypothesis that by instituting this protocol we could reduce complication rates in patients undergoing LEB.

## METHODS

**Patients and databases.** We used prospectively collected data from the VSGNE, a regional cooperative group dedicated to quality assessment and improvement in vascular surgery.<sup>18</sup> The VSGNE quality vehicle was used at a single institution to measure a change in clinical practice. All patients undergoing LEB in our institution after January 2009 were treated with an IV insulin protocol. All patient information was entered prospectively into the VSGNE database and was later retrospectively queried and compared to a historic control population. The historic control population was comprised of all patients treated with LEB at our institution from 2006 to 2008 before the start of our pilot study.

Consecutive patients undergoing elective, urgent, or emergent open infrainguinal LEB for occlusive or aneurysmal disease were included. Both diabetics and nondiabetics were placed on standard insulin therapy before January 2009 and on intensive IV insulin treatment after that time period. Indications for LEB included both claudication and critical limb ischemia. A number of conduit types were used, including vein, prosthetic, or composite grafts. Vein harvests were performed as open procedures. Patients with previous percutaneous transluminal angioplasty and/or stents were included in the study. Supra-inguinal revascularizations, extra-anatomic bypasses, and revascularizations for trauma were excluded from analysis. Hospital protocol dictates that preoperative preparation includes skin clipping with no razors and skin preparation. Skin preparations differed according to surgeon preference or as an allergy-directed scrub. First-generation cephalosporin was given 1 hour before skin incision.

The institutional review board at the University of Vermont reviewed the VSGNE program run by the Vascular Surgery Department and found it to fit under the oversight of the James M. Jeffords Institute for Quality and Operational Effectiveness at Fletcher Allen Health Care. The use of IV insulin represents a practice change that we have reviewed periodically via the VSGNE vehicle.

**Continuous IV insulin protocol.** Patients who were placed on the IV insulin protocol received continuous IV insulin immediately postoperatively and continued for 72 hours (Appendix I, online only). The insulin infusion was initiated when the finger stick blood glucose (FSBG) reached  $\geq 120$  mg/dL, with a target titration goal between 80 and 150 mg/dL. If the FSBG was within this target range, the FSBG was initially checked every hour. After 6 hours of glucoses within this range, the monitoring was lengthened to every 2 hours. If the first postoperative FSBG was  $< 120$  mg/dL, the glucose level was checked every 2 hours. If the initiation goal of  $\geq 120$  mg/dL was not reached after 6 hours, the patient was switched to standard insulin coverage with FSBG levels obtained four times daily before meals and at bedtime.

To prevent hypoglycemia, the infusion was decreased by 50% if the glucose level decreased below 80 mg/dL and held if the level dropped below 66 mg/dL with the addition of 12.5 g of D50 IV push or 15 g of oral carbohydrates. If glucose levels dropped to  $< 66$  mg/dL, an FSBG was rechecked every 30 minutes. If the glucose level was between 66 and 79 mg/dL, an FSBG was checked every hour.

During periods of hyperglycemia, the insulin drip was adjusted so that the infusion was increased by 1 unit/hour once the glucose level reached  $> 150$  mg/dL, and it was increased by 2 units/hour if  $> 250$  mg/dL, to a maximum of 20 units/hour. When glucose levels were between 151 and 499, FSBG was checked every 2 hours. If the glucose level increased to  $> 500$  mg/dL, the FSBG was rechecked in 1 hour.

**Standard insulin protocol.** Diabetic and nondiabetic historic controls who underwent LEB from 2006 to 2008 were placed on a standard insulin protocol. Standard treatment can be defined as best medical therapy for the patient's comorbidities. Postoperatively, patients in the historic control group resumed their normal preoperative home regimen of antidiabetic medications (if they had been on medications). If during the postoperative period they became hyperglycemic and met parameters for the institution of insulin, they were placed on a supplemental insulin aspart sliding scale adjusted based on their nutritional status, blood glucose level, age, weight, and serum creatinine (Appendix II, online only). If the patient was not receiving nutritional intake by mouth, FSBG checks were implemented every 6 hours. Once the patient was tolerating nutritional intake, FSBG checks were performed four times daily before meals and at bedtime. If the patient had an established home insulin regimen, they were restarted on their normal doses once they resumed eating in addition to the insulin aspart sliding scale. Hypoglycemia prevention consisted of a 12.5-g D50 IV push if the FSBG decreased to  $< 66$  mg/dL.

**Outcome measures.** The primary outcome measures were in-hospital wound infection after LEB. According to the VSGNE database, a wound infection is defined as the initiation of antibiotic treatment or positive culture. Clinical suspicion based on physical examination findings in-

cluded, but were not limited to, presence of erythema, fever, or drainage from the wound site. Graft infection according to the VSGNE is cited if antibiotics were initiated or with documentation of exposed graft or graft infection in the medical records. Secondary outcomes measured included blood transfusion requirement, myocardial infarction, new dysrhythmia, congestive heart failure, respiratory complication, amputation, length of stay, discharge ankle-brachial and toe-brachial index, palpable graft pulse, palpable distal pulse, increase in ankle-brachial index  $>0.15$ , and duplex imaging. Return to the operating room for bleeding, thrombosis, infection, or revision was also recorded.

**Statistics.** Baseline patient characteristics and outcome measures were evaluated using the Fisher exact test and  $\chi^2$  analysis for categorical data, two-sample *t*-test for continuous variables that were normally distributed, and Wilcoxon rank-sum test for non-normal continuous variables. Logistic regression analysis was used to adjust for potential confounders such as body mass index (BMI), gender, and smoking status. Stratified analyses were further completed to look for differences that could be explained by the presence or absence of diabetes. All statistical tests were two-tailed and deemed significant if  $P < .05$ .

## RESULTS

One hundred eighty-nine historic controls that underwent LEB and were placed on standard insulin therapy were evaluated. One hundred nineteen study patients were placed on postoperative IV insulin during the time period and were eligible for the study. Of the 119 patients in the IV insulin group, 15 (13%) were excluded due to surgeon preference ( $n = 2$ ), incomplete data ( $n = 10$ ), and lack of protocol adherence ( $n = 3$ ), resulting in a total of 104 patients in the IV insulin study group.

**Total patient population with lower extremity bypass.** There were no baseline differences between the two groups with regard to preoperative characteristics, except patients in the historic control group had a higher BMI and an increased rate of prior and current smoking compared to the IV insulin group ( $P = .005$  and  $.001$ ), and patients in the IV insulin group were more likely to be on a preoperative statin and aspirin ( $P = .004$  and  $P = .02$ ; Table). In the IV insulin group, five patients (5%) had their diabetes controlled preoperatively with diet, 14 (13%) with oral medications, and 25 (24%) with insulin. Within the historic control group, 15 patients (8%) had their diabetes controlled with diet, 32 (17%) with oral medications, and 43 (23%) with insulin. There was no significant difference between the two groups ( $P = .63$ ). There were no differences in the indication for surgery, graft type, or timing of the operation.

A total of 21 patients in the historic control group and four patients in the IV insulin group developed postoperative wound infections. Out of the patients who developed postoperative wound infections, six of 21 (30%) in the historic control group and one of four (25%) in the IV insulin group had preoperative wound infections ( $P = 1.00$ ). Patients in the IV insulin group had significantly

fewer wound infections compared with patients in the historic control group (4% vs 11%; odds ratio [OR], 0.32; 95% confidence interval [CI], 0.11-0.96;  $P = .047$ ). The association remained significant in multivariate analyses adjusting for BMI, gender, and smoking status (OR, 0.22; 95% CI, 0.05-0.84;  $P = .03$ ). Adjusting for statin use, aspirin use, and prosthetic vs vein graft did not change the relationship between IV insulin use and postoperative wound infection. The 15 patients excluded who were on IV insulin and the 104 patients included who were on IV insulin were compared on 91 variables. The only significant differences were that the 15 excluded patients were less likely to be diabetic (93% nondiabetic compared to 58% nondiabetic for the 104 included;  $P = .02$ ), more likely to have had a previous left leg bypass (53% vs 13% for the 104 included;  $P = .001$ ), and lower BMI (mean of 24.7 vs 27.3 for the 104 included;  $P = .04$ ). When those 15 patients were included in the analysis, the relationship between IV insulin use and wound infection was slightly stronger than when they were excluded (4% of IV insulin vs 11% in the historic control group;  $P = .036$ ). Therefore, their exclusion does not affect the observed IV insulin vs wound infection relationship. Patients in the IV insulin group had a decreased length of stay of 5.9 days compared to 6.5 days for patients in the historic control group, however, the results were nonsignificant ( $P = .86$ ).

Patients with postoperative wound infections had a significantly longer length of stay (10.7 vs 5.9 days;  $P < .001$ ). Patients with postoperative wound infections in the IV insulin group showed a trend toward an increased length of stay compared to those without wound infections (8.0 vs 5.8 days), however, this difference was only marginally significant ( $P = .05$ ). Patients in the historic control group with postoperative wound infections had an increased mean length of stay of 11.2 days compared with 5.9 days for patients without wound infections ( $P = .003$ ; Fig 1).

There were no differences in the rates of postoperative graft infections, transfusions, myocardial infarctions, dysrhythmias, congestive heart failure, or respiratory complications (Fig 2). One patient in the historic control group developed a wound infection after blood transfusion. There was no association between return to the operating room for bleeding or thrombosis and the incidence of postoperative wound infection (8% vs 9%;  $P = 1.00$ ). Hypoglycemia (glucose  $<60$  mg/dL) occurred in 19% (20/104; 95% CI, 0.12-0.28) of patients on the insulin infusion without any clinically evident complications.

**Diabetic population.** Patients with diabetes in the IV insulin group had significantly less wound infections than patients without diabetes in the historic control group (Fig 3). None of the patients with diabetes in the IV insulin group developed postoperative wound infections compared with 10% of patients with diabetes in the historic control group ( $P = .03$ ). There was also a trend toward a decreased length of stay among patients with diabetes in the IV insulin group compared to patients with diabetes in the historic control group (6.8 vs 8.6 days;  $P = .26$ ).

**Table.** Patient characteristics

	<i>IV insulin</i>		<i>Historic control</i>		<i>P value</i>
	<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>	
Gender					
Male	83	81	140	74	.25
Age					
Mean (SD)	64.3	9.70	65.2	11.60	.5
BMI					
Mean (SD)	27.3	4.50	29.2	6.10	.005
Smoking					
Never	7	7	21	11	.001
Prior	48	46	121	64	
Current	49	47	47	25	
HTN					
Yes	86	83	160	85	.74
Diabetes					
None	60	58	99	52	.63
Diet	5	5	15	8	
Oral medications	14	13	32	17	
IV insulin	25	24	43	23	
CABG/PTCA					
None	73	70	134	71	.89
<5 years	20	19	38	20	
>5 years	11	11	17	9	
CHF					
Yes	2	2	9	5	.34
COPD					
No	87	84	162	86	.35
Not treated	9	9	9	5	
On medications	7	7	17	9	
Dialysis					
No	100	96	183	97	.87
Dialysis	3	3	4	2	
Transplant	1	1	2	1	
Pre-op ASA					
Yes	97	95	162	86	.02
Pre-op Plavix					
Yes	2	2	8	4	.5
Pre-op statin					
Yes	82	81	122	65	.004
Indication					
Asymptomatic	11	11	20	11	.27
Claudication	34	33	40	21	
Rest pain	30	29	54	29	
Tissue loss	26	25	64	34	
Acute ischemia	3	3	8	4	
Not treated	0	0	2	1	
Graft					
Vein	78	75	158	84	.09
Prosthetic	26	25	31	16	
Urgency					
Elective	95	91	164	87	.37
Urgent	8	8	18	10	
Emergent	1	1	7	4	

ASA, Acetylsalicylic acid (aspirin); BMI, body mass index; CABG, coronary artery bypass; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HTN, hypertension; IV, intravenous; PTCA, percutaneous transluminal coronary angioplasty.

**Nondiabetic population.** In nondiabetics treated with IV insulin, there were less wound infections compared to those in the historic control group, however, the difference was not statistically significant (7% vs 12%;  $P = .42$ ). There was no difference in the length of stay for nondiabetics on IV insulin (5.3 vs 4.6 days;  $P = .27$ ).

## DISCUSSION

Blood glucose levels are elevated postoperatively secondary to stress-induced production of catecholamines elicited by surgery. Although hyperglycemia and diabetes are oftentimes indivisibly linked, it is unclear whether it is the diabetic state or whether hyperglycemia in and of itself

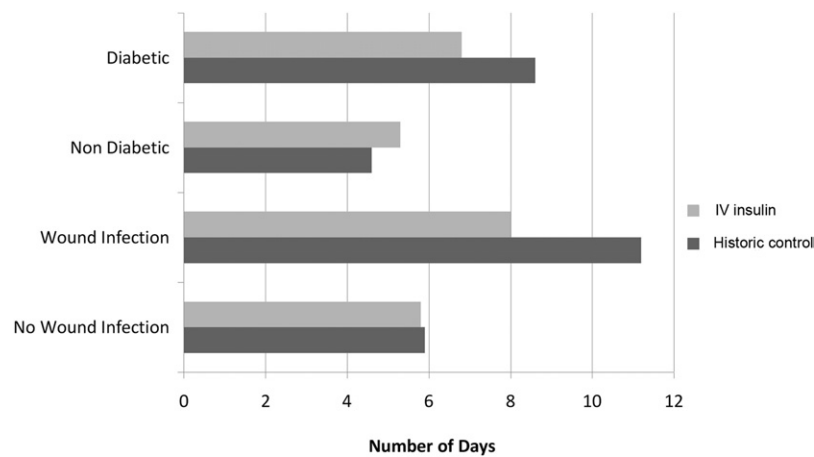


Fig 1. Length of stay. *IV*, Intravenous.

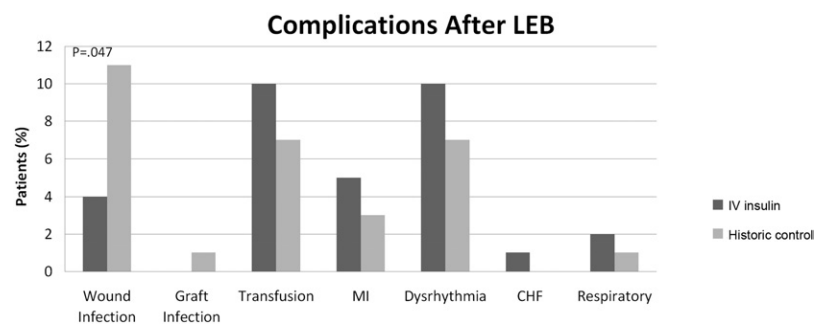


Fig 2. Postoperative complications. *CHF*, Congestive heart failure; *IV*, intravenous; *LEB*, lower extremity bypass; *MI*, myocardial infarction.

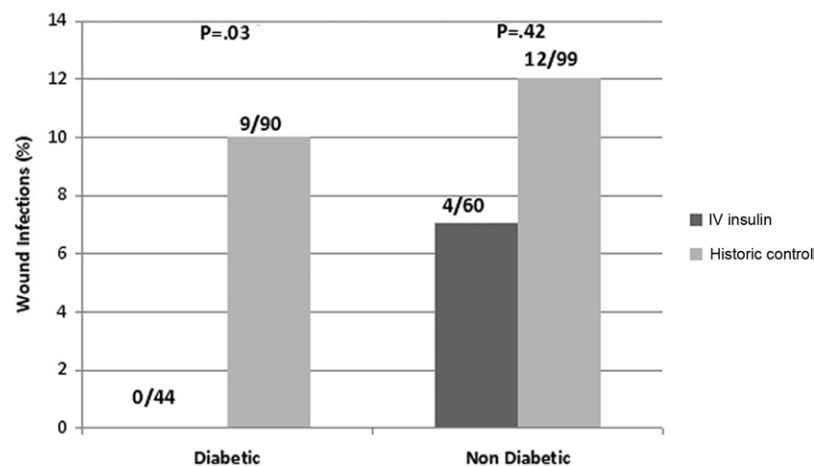


Fig 3. Wound infections among diabetic and nondiabetic patients based on therapy. *IV*, Intravenous.

contributes to poor wound healing. Postoperative hyperglycemia is an independent risk factor for wound infections among cardiothoracic patients with and without diabetes with a direct correlation between the degree of glucose

elevation and risk of infection.<sup>2,19,20</sup> Our study did not find a statistical difference in the rate of wound infections among diabetic compared to nondiabetic patients receiving *IV* insulin, and it is unclear if strict perioperative glycemic



control is as beneficial in the nondiabetic population as it is for the diabetic population in the face of surgically induced hyperglycemia.

The outcomes of tight glycemic control and incidence of wound infections are not well documented in vascular surgery patients. A retrospective study by Ramos et al<sup>21</sup> examining diabetic and nondiabetic patients undergoing general and vascular surgery found that postoperative hyperglycemia increased the risk of postoperative infection (pneumonia, urinary tract infections, wound infections, and sepsis) by 30% with every 40 mg/dL increase from normoglycemia. Our study revealed that patients undergoing LEB with strict postoperative glycemic control had significantly decreased wound infections. Furthermore, patients with diabetes receiving IV insulin had significantly less wound infections compared to patients with diabetes in the historic control group treated with standard insulin therapy.

The application of intensive insulin therapy is accompanied by the potential for hypoglycemia-related events. The NICE-SUGAR trial revealed that strict glycemic control (81–108 mg/dL) increased mortality among critically ill patients.<sup>22</sup> Subramaniam et al<sup>4</sup> found that episodes of hypoglycemia were 3.1% vs 4.1% among vascular surgery patients on intensive insulin therapy compared to standard therapy, respectively, with no clinically evident symptoms. Nineteen percent (20/104) of our patients in the IV insulin protocol had hypoglycemia (glucose <60 mg/dL), with no episodes of severe hypoglycemia (glucose <40 mg/dL). Neither mild nor severe clinical manifestations of hypoglycemia were experienced among our study subjects. Our small sample size is a limitation in determining the extent of the potential consequences of hypoglycemia. This study demonstrates the benefits of decreased wound infections in the subgroup of patients with diabetes placed on IV insulin, however, it is indeterminate if strict glucose control in nondiabetics is as advantageous.

Despite the risk of hypoglycemic events, tight glycemic control may improve patient outcomes by reducing length of stay. Studies have demonstrated a correlation between hyperglycemia and increased length of hospitalization.<sup>6,21</sup> Within our population, patients with postoperative wound infections had a significantly longer length of hospital stay compared to patients without a postoperative wound infection. Patients with diabetes on IV insulin showed a trend toward a shorter length of stay compared to patients with diabetes in the IV insulin group suggesting an additional benefit to the use of tight glycemic control within the postoperative period.

This study had several limitations, including its small sample size and observational design. Although the data were collected prospectively, historic controls were used for comparison purposes. However, there were few differences in patient characteristics between the two groups, and adjusting for these differences did not change the findings. We estimate a trial of over 1800 patients is needed to detect a 50% reduction of in-hospital wound infections at 80% power. This pilot study serves as proof of concept to justify

a randomized controlled trial of glucose control after LEB. We likely underestimated the rate of wound infections because a significant number of wound infections present after discharge. Furthermore, the complications associated with hypoglycemic events may not have been diagnosed at the time or documented appropriately.

## CONCLUSIONS

Strict glycemic control with a postoperative insulin infusion protocol significantly decreased the incidence of in-hospital postoperative wound infection in patients undergoing LEB. In subpopulation analysis, patients with diabetes benefited from the use of this protocol more than other populations studied. It is our belief that the use of an IV insulin protocol can help reduce complications in the diabetic population.

## AUTHOR CONTRIBUTIONS

Conception and design: AS

Analysis and interpretation: JA, PC, DB, GS, AS

Data collection: JA, DB, GS, JM, AS

Writing the article: FH, RP

Critical revision of the article: JA, PC, DB, AS

Final approval of the article: FH, RP, JA, PC, DB, AS

Statistical analysis: PC

Obtained funding: AS

Overall responsibility: AS

## REFERENCES



1. Furnary AP, Gao G, Grunkemeier GL, Wu Y, Zerr KJ, Bookin SO, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003;125:1007–21.
2. Lazar HL, Chipkin SR, Fitzgerald CA, Bao Y, Cabral H, Apstein CS. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation* 2004;109:1497–502.
3. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001;345:1359–67.
4. Subramaniam B, Panzica PJ, Novack V, Mahmood F, Matyal R, Mitchell JD, et al. Continuous perioperative insulin infusion decreases major cardiovascular events in patients undergoing vascular surgery: a prospective, randomized trial. *Anesthesiology* 2009;110:970–7.
5. Chaney MA, Nikolov MP, Blakeman BP, Bakhos M. Attempting to maintain normoglycemia during cardiopulmonary bypass with insulin may initiate postoperative hypoglycemia. *Anesth Analg* 1999;89:1091–5.
6. Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, O'Brien PC, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med* 2007;146:233–43.
7. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunol Med Microbiol* 1999;26:259–65.
8. Mowat A, Baum J. Chemotaxis of polymorphonuclear leukocytes from patients with diabetes mellitus. *N Engl J Med* 1971;284:621–7.
9. Guerci B, Böhme P, Kearney-Schwartz A, Zannad F, Drouin P. Endothelial dysfunction and type 2 diabetes. Part 2: altered endothelial function and the effects of treatments in type 2 diabetes mellitus. *Diabetes Metab* 2001;27(4 Pt 1):436–47.
10. Lash JM, Nase GP, Bohnen HG. Acute hyperglycemia depresses arteriolar NO formation in skeletal muscle. *Am J Physiol* 1999;277(4 Pt 2):H1513–20.

11. Park JY, Takahara N, Gabriele A, Chou E, Naruse K, Suzuma K, et al. Induction of endothelin-1 expression by glucose: an effect of protein kinase C activation. *Diabetes* 2000;49:1239-48.
12. Rayfield EJ, Ault MJ, Keusch GT, Brothers MJ, Nechemias C, Smith H. Infection and diabetes: the case for glucose control. *Am J Med* 1982; 72:439-50.
13. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Contr* 1999;27:97-132; quiz: 133-4; discussion 96.
14. Noorani A, Rabey N, Walsh SR, Davies RJ. Systematic review and meta-analysis of preoperative antisepsis with chlorhexidine versus povidone-iodine in clean-contaminated surgery. *Br J Surg* 2010;97: 1614-20.
15. McIntosh J, Earnshaw JJ. Antibiotic prophylaxis for the prevention of infection after major limb amputation. *Eur J Vasc Endovasc Surg* 2009;37:696-703.
16. Vascular Study Group of New England. Available at: <http://www.vascularweb.org/regionalgroups/vsgne/Pages/home.aspx>.
17. Bertges DJ, Goodney PP, Zhao Y, Schanzer A, Nolan BW, Likosky DS, et al. The Vascular Study Group of New England cardiac risk index (VSG-CRI) predicts cardiac complications more accurately than the revised cardiac risk index in vascular surgery patients. *J Vasc Surg* 2010;52:674-83.
18. Cronenwett JL, Likosky DS, Russell MT, Eldrup-Jorgensen J, Stanley AC, Nolan BW, et al. A regional registry for quality assurance and improvement: the Vascular Study Group of northern New England (VSGNNE). *J Vasc Surg* 2007;46:1093-101; discussion: 1101-2.
19. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Contr Hosp Epidemiol* 2001;22:607-12.
20. Swenne CL, Lindholm C, Borowiec J, Schnell AE, Carlsson M. Perioperative glucose control and development of surgical wound infections in patients undergoing coronary artery bypass graft. *J Hosp Infect* 2005;61:201-12.
21. Ramos M, Khalpey Z, Lipsitz S, Steinberg J, Panizales MT, Zinner M, et al. Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. *Ann Surg* 2008;248:585-91.
22. NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY, Blair D, Foster D, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360:1283-97.

Submitted Oct 29, 2011; accepted Jan 4, 2012.

*Additional material for this article may be found online at [www.jvascsurg.org](http://www.jvascsurg.org).*

Appendix I (online only). Continuous intravenous insulin protocol

 <small>In alliance with The University of Vermont</small>		MRN _____ Name _____ DOB _____
<b>PHYSICIANS ORDER SHEET -</b> <b>NON - ICU Insulin Infusion Protocol 036224</b> Not for DKA or HHS		
Page 1 of 1		Addressograph _____
Hospital policy dictates that all orders list substances to be avoided. ALLERGIES / SUBSTANCES TO BE AVOIDED: (include allergies to drugs, food, latex, etc).		
<input type="checkbox"/> None known <input type="checkbox"/> Avoid/Reason _____		
<b>I. Insulin Infusion</b> (Circle A or B) (HIS P270) Note: Pharmacy will dispense regular insulin 1 unit/mL in NS IV infusion		
A. Initiate insulin infusion per Non-ICU Insulin Infusion Protocol		
1. Do not start insulin infusion until potassium is verified > 3.5 mEq/ml. Potassium = _____		
2. Do not start insulin infusion until glucose is $\geq 120$ mg/dl		
3. If glucose < 120 mg/dl, monitor glucose every 2 hours X 6 hours. If during this 6 hour period glucose is $\geq 120$ mg/dl initiate insulin infusion. If after 6 hours, glucose is still < 120 mg/dl, begin AC and bedtime monitoring		
4. Begin an infusion of normal saline at 10 ml/hr with the insulin infusion		
B. Continue insulin infusion at a rate of _____ units/hour on arrival to non-ICU floor		
1. Begin an infusion of normal saline at 10 ml/hr with the insulin infusion		
• Blood glucose monitoring and titration of insulin infusion per protocol guidelines		
<b>II. Caloric Support for Patients Not Receiving Any Nutrition</b> : (Circle A, B, or C) Note: A patient who is NPO or not receiving any nutritional support such as tube feeding, TPN, or IV Dextrose <b>must</b> have caloric support while on an insulin infusion		
A . D10W infusion at 80 ml/hr		
B . D5W infusion at _____ ml/hr		
C. Other _____		
<b>III. Scheduled Nutritional Subcutaneous Insulin:</b> (Circle A or B) Note: Patients on solid food should be on a carbohydrate controlled diet.		
A. Administer subcutaneous aspart insulin with meals per Non-ICU Insulin Infusion Protocol (HIS P270A)		
B. Do not administer subcutaneous insulin with meals (HIS P270B)		
• Notify prescriber of post prandial glucose > 180 mg/dL. This is an indication for the need to add nutritional insulin coverage.		
<b>IV. Hypoglycemia Prevention</b>		
• If nutritional support (PO, TPN, PPN, tube feeding) has unplanned interruption, check glucose q 1 hour x 4 hours then resume previous frequency if glucose > 80 mg/dL		
• Notify prescriber immediately and start D10 at 80ml/hr		
NOTE: Insulin deficient patients require basal insulin ( i.e. NPH, glargine, insulin drip or insulin pump) to prevent diabetic ketoacidosis. Sliding scale insulin alone is discouraged per ADA Inpatient Glycemic Control Guide		
Date: _____ Time: _____ Beeper/Contact No.: _____ Signature: _____		
 LIP		_____
FM NO. 036224 (Revised 08/2008)		Print Name _____
White Copy (Chart)		



## Appendix I (online only). Continued.

**Starting rate of insulin:**

Start insulin infusion based on chart below. All insulin infusion starts need a second nurse check

Starting blood glucose	Receiving caloric intake*	Rate of insulin infusion
120 – 220 mg/dL	NO	1 unit/hour
120 – 220 mg/dL	YES	2 unit/hour
> 220 mg/dL	Either yes or no	4 unit/hour

\*Caloric intake: includes continuous D10 or D5W infusion, TPN, PPN, tube feeding, or a po diet

**Blood glucose monitoring:** At any point, a nurse can initiate more frequent monitoring

- Blood glucose to be checked prior to starting infusion and at minimum q 1 hour X 6 hours
- After 6 hourly checks:
  - If FSBG is within range (80 – 150 mg/dL) recheck in 2 hours and then per infusion chart below
  - If FSBG is NOT within range please consult prescriber

Titration of insulin infusion – refer to chart below (\*\*Critical lab values are FSBG &lt;50 or &gt; 500 mg/dL)

BG results	Nursing action	Infusion rate adjustment	Minimum BG frequency –
< 41 mg/dL	Give 25 gm D50 IVP (50 ml) stat Notify LIP*	Hold insulin infusion Restart infusion at 50% of previous rate when glucose > 100 mg/dL	Recheck FSBG q 30 minutes
41 – 65 mg/dL**	Give 12.5 gm D50 (25 mL) OR 15 gm CHO po. Notify LIP if < 50mg/dL or if D50 administered	Hold insulin infusion Restart infusion at 50% of previous rate when glucose > 100 mg/dL	Recheck FSBG q 30 minutes
66 – 79 mg/dL		Decrease infusion by 50%	Check FSBG q 1 hour
80 – 100 mg/dL		Continue at current rate	Check FSBG q 1 hour May advance to q 2 hours after 6 hours of glucose within range
101 – 150 mg/dL		Continue at current rate	If FSBG decreases > 25 mg/dL from previous reading check FSBG in 1 hour May advance to q 2 hours after 6 hours of glucose within range
151 – 250 mg/dL	Call LIP if 3 consecutive values occur in this range	Increase infusion by 1 unit per hour	Recheck blood glucose in 2 hours Note: If blood glucose is <200 and the decrease from the last blood glucose was more than 50 mg/dL, DO NOT increase drip rate. Recheck glucose in one hour.
251 – 500 mg/dL	Call LIP if 3 consecutive values occur in this range	Increase infusion by 2 unit per hour	Recheck blood glucose in 2 hours
> 500 mg/dL **	Notify LIP. Obtain stat serum Glc, lytes, ketones. Check lytes and ketones once in 24 hours	Per LIP	All > 500 mg/dL values require a lab draw confirmation Recheck in 1 hour

\*LIP: Licensed independent practitioner including MD, nurse practitioner, physician assistant

Titrate insulin infusion between 0 – 20 units/hour per titration chart above.

- Notify prescriber if  $\geq 20$  units/hr is required to control glucose
- All insulin infusion titrations require a second nurse validation
- Discontinue infusion if rate is < 0.5 units/hour. Recheck glucose in 1 hour
  - If < 120 mg/dL contact prescriber
  - If  $\geq 120$  mg/dL resume insulin infusion at 0.5 units/hour

**Nutritional coverage:** Per MD order page 1**A. Subcutaneous Aspart insulin:** Used to prevent post-prandial glucose elevation

- Administer immediately after the patient has eaten meal
- Do not administer if pt is NPO, does not eat, or is severely nauseated after eating

Premeal infusion rate (units/hr)	Intake > 50% of meal	Intake < 50% of meal
1 – 2	4 units	2 units
2.1 – 4	6 units	3 units
4.1 – 6	8 units	4 units
6.1 – 8	10 units	5 units
8.1 – 10	12 units	6 units
> 10 units	14 units	7 units

**Transition from IV insulin infusion to subcutaneous insulin regimen**

Prior to discontinuing IV insulin infusion, contact prescriber for scheduled subcutaneous insulin orders

**Transport off unit:** Check BG before patient leaves. Accompany patient off unit and continue protocol

## Appendix II (online only). Standard insulin protocol

### A. Physician notification:

- Automatic assessment and action - critical laboratory values are finger-stick blood glucose (FSBG) <50 mg/dL or >500 mg/dL. FSBG values >500 mg/dL require serum blood glucose (BG) confirmation. If FSBG <50 mg/dL, do not delay treatment.
- If eating, FSBG checked four times daily before meals and at bedtime.
- If NPO, glucose check Q6.
- If FSBG <66 mg/dL and patient cannot swallow or is NPO.
- Administer 25 mL D50 intravenous (IV) push stat and call LP. Recheck FSBG in 15 minutes and 60 minutes for response.
- If FSBG is <66 mg/dL in the AM, treat as above and recheck FSBG at 0200 for 2 nights.
- If FSBG is <66 mg/dL  $\times$  2 in the last 6 hours treat as above and call LP.

### B. FSBG checks

### C. Hypoglycemia prevention

### D. Bedtime FSBG:

- If bedtime FSBG >250 mg/dL, 5 units of supplemental insulin will be given and FSBG will be rechecked at midnight.

### E. Supplemental insulin aspart protocol if patient is NPO <24 hours:

Critical values are FSBG <50 mg/dL or >500 mg/dL.

#### Dosing regimen for SCr >3.5, age >80

FSBG	Units of insulin aspart
66-140	0
141-180	0
181-210	1
211-250	2
251-299	3
>299	5

#### Dosing regimen weight between 50 and 75 kg

FSBG	Units of insulin aspart
66-140	0
141-180	1
181-210	2
211-250	4
251-299	6
>299	9

#### Dosing regimen weight between 76 and 100 kg

FSBG	Units of insulin aspart
66-140	0
141-180	2
181-210	3
211-250	5
251-299	7

## Appendix II (online only). Continued.

FSBG	Units of insulin aspart
>299	11

#### Dosing regimen weight between 101 and 125 kg

FSBG	Units of insulin aspart
66-140	0
141-180	3
181-210	4
211-250	6
251-299	8
>299	12

#### Dosing regimen weight >125 kg

FSBG	Units of insulin aspart
66-140	0
141-180	4
181-210	5
211-250	7
251-299	9
>299	13

## SUPPLEMENTAL INSULIN ASPART WHEN PATIENT IS EATING

#### Dosing regimen for SCr >3.5, age >80

FSBG	Units of insulin aspart
66-140	0
141-180	0
181-210	1
211-250	2
251-299	3
>299	5

#### Dosing regimen weight between 50 and 75 kg

FSBG	Units of insulin aspart
66-140	0
141-180	1
181-210	2
211-250	4
251-299	6
>299	9

#### Dosing regimen weight between 76 and 100 kg

FSBG	Units of insulin aspart
66-140	0
141-180	2
181-210	3
211-250	5
251-299	7
>299	11

**Appendix II (online only).** Continued.  
Dosing regimen weight between 101 and 125 kg

<i>FSBG</i>	<i>Units of insulin aspart</i>
66-140	0
141-180	3
181-210	4
211-250	6
251-299	8
>299	12

**Appendix II (online only).** Continued.  
Dosing regimen weight >125 kg

<i>FSBG</i>	<i>Units of insulin aspart</i>
66-140	0
141-180	4
181-210	5
211-250	7
251-299	9
>299	13